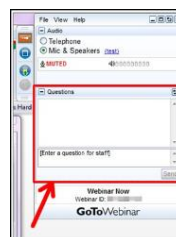




Have Questions?



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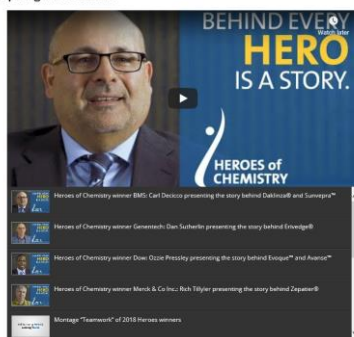
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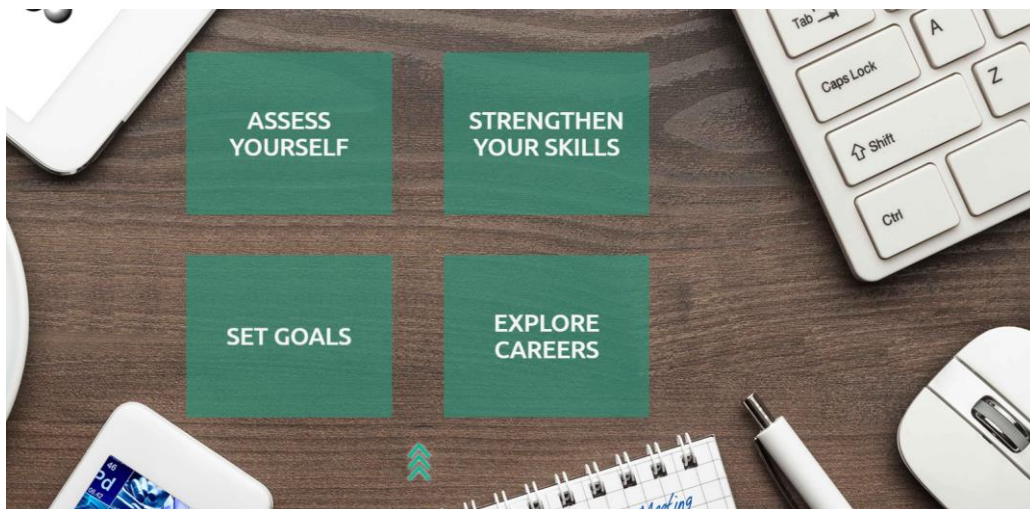
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An individual development  
planning tool for you!

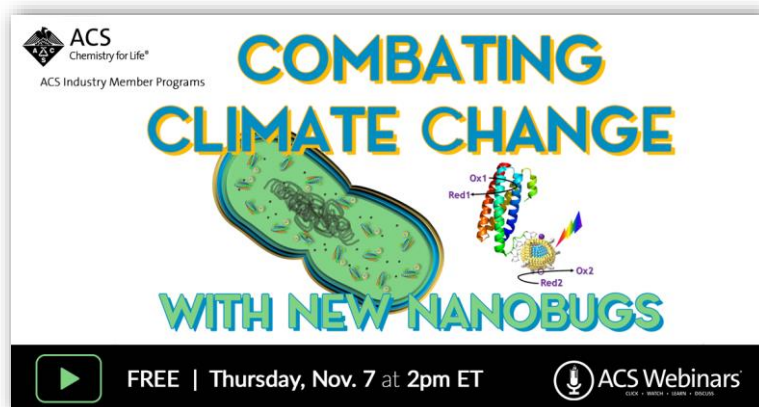


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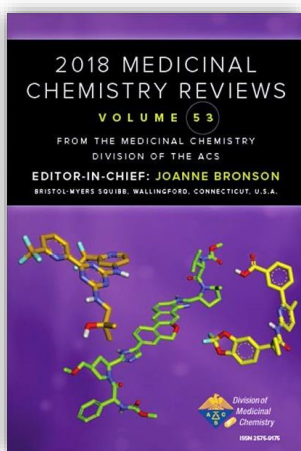
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| 2014                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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| <p><b>Drug Discovery Series #1 - Current Drug Discovery and Development Process</b><br/>QD1 #1 Watch the overview of the drug discovery and development process from the drug and challenges in early R&amp;D.</p> <p><b>Primer in Drug Target Classes</b><br/>QD1 #2 Learn in a discussion on the big four drug target families and the difference between small molecule and biologics targets.</p> <p><b>Key Concepts in Identifying Drug Leads</b><br/>QD1 #3 Discover how drug targets are a starting point, explore the A to Z of drug and how new targets from the past have guided the present.</p> <p><b>Lead Optimization - Building Efficacy &amp; Safety</b><br/>QD1 #4 Learn strategies on how to effectively optimize and maintain hit and rapidly assess your findings.</p> <p><b>Tip for Hitting H2O and Starting your Clinical Trials</b><br/>QD1 #5 How do you need to cross over from pre-clinical to Phase I drug submissions to the United States Food and Drug Administration?</p> <p><b>The Role of Chemistry in Clinical Trials: The Big Expense &amp; Lessons Learned</b><br/>QD1 #6 Learn how the properties of the molecule impact decisions in the discovery process.</p> <p><b>Pharmacokinetics and IP Strategies in Drug Development</b><br/>QD1 #7 Review the basic principles of Pharmacokinetics in drug development strategies as well as to risk in determining health insurance coverage of drug products.</p> <p><b>Future of Drug Discovery - Challenges, Risks and Rewards</b><br/>QD1 #8 Explore how new ideas and challenges will be dealt with in the future and the key role required of future medicinal chemists.</p> | <p><b>Designing Better Drug Candidates</b><br/>QD1 #9 Learn about factors that can be used to improve candidate quality from 2D to 3D.</p> <p><b>Strategies to Improve Solubility of Drug Candidates</b><br/>QD1 #10 Learn a number of different strategies for improving drug solubility through structural modification.</p> <p><b>Fragment Based Drug Design Strategies</b><br/>QD1 #11 Design the right drug target to maximize fragment efficiency. Learn how to focus on the target protein and how to use it.</p> <p><b>Screening Strategies</b><br/>QD1 #12 Learn the pros and cons of different screening strategies.</p> <p><b>Assessing 3D5D Protein-DNA Interactions</b><br/>QD1 #13 Learn how to use computational tools to assess the drug target.</p> <p><b>Assessing 3D5D Protein-DNA Interactions</b><br/>QD1 #14 Learn how to use computational tools to assess the drug target.</p> <p><b>Assessing 3D5D Protein-DNA Interactions</b><br/>QD1 #15 Learn how to use computational tools to assess the drug target.</p> <p><b>Assessing 3D5D Protein-DNA Interactions</b><br/>QD1 #16 Learn how to use computational tools to assess the drug target.</p> <p><b>Assessing 3D5D Protein-DNA Interactions</b><br/>QD1 #17 Learn how to use computational tools to assess the drug target.</p> <p><b>Assessing 3D5D Protein-DNA Interactions</b><br/>QD1 #18 Learn how to use computational tools to assess the drug target.</p> <p><b>Assessing 3D5D Protein-DNA Interactions</b><br/>QD1 #19 Learn how to use computational tools to assess the drug target.</p> <p><b>Assessing 3D5D Protein-DNA Interactions</b><br/>QD1 #20 Learn how to use computational tools to assess the drug target.</p> | <p><b>1- Target: The Fourth Dimension in Drug Discovery</b><br/>The Importance of Drug Target Modulation in Drug Design<br/>Robert Copeland - Bristol-Myers Squibb<br/>Dan Stanton - Bristol-Myers Squibb</p> <p><b>2- Target: The Fourth Dimension in Drug Discovery</b><br/>Long Acting Injectable Medications: Strategies and Mechanisms<br/>Amrita Bak - AstraZeneca</p> <p><b>3- Target: The Fourth Dimension in Drug Discovery</b><br/>Modified Release Formulations for Solubility Stained Compounds<br/>Vijay Kumar - AstraZeneca</p> <p><b>4- Target: The Fourth Dimension in Drug Discovery</b><br/>The Molecular Design of Transmembrane Protein<br/>Benjamin Kuchel - AstraZeneca</p> <p><b>5- Target: The Fourth Dimension in Drug Discovery</b><br/>Rational Design of Small Molecules<br/>Scott L. Schreiber - AstraZeneca</p> <p><b>6- Target: The Fourth Dimension in Drug Discovery</b><br/>Designing Drug Target Modulation in Drug Design<br/>Scott L. Schreiber - AstraZeneca</p> <p><b>7- Target: The Fourth Dimension in Drug Discovery</b><br/>Designing Drug Target Modulation in Drug Design<br/>Scott L. Schreiber - AstraZeneca</p> <p><b>8- Target: The Fourth Dimension in Drug Discovery</b><br/>Designing Drug Target Modulation in Drug Design<br/>Scott L. Schreiber - AstraZeneca</p> <p><b>9- Target: The Fourth Dimension in Drug Discovery</b><br/>Designing Drug Target Modulation in Drug Design<br/>Scott L. Schreiber - AstraZeneca</p> <p><b>10- Target: The Fourth Dimension in Drug Discovery</b><br/>Designing Drug Target Modulation in Drug Design<br/>Scott L. Schreiber - AstraZeneca</p> | <p><b>1- Fighting Cancer</b><br/>Fighting Cancer: Targeting Cytotoxicity with Kinase Inhibitors<br/>Timothy D. Haffner - AstraZeneca</p> <p><b>2- Fighting Cancer</b><br/>Fighting Cancer: Targeting Cytotoxicity with Kinase Inhibitors<br/>Timothy D. Haffner - AstraZeneca</p> <p><b>3- Fighting Cancer</b><br/>Fighting Cancer: Targeting Cytotoxicity with Kinase Inhibitors<br/>Timothy D. Haffner - AstraZeneca</p> <p><b>4- Fighting Cancer</b><br/>Fighting Cancer: Targeting Cytotoxicity with Kinase Inhibitors<br/>Timothy D. Haffner - AstraZeneca</p> <p><b>5- Fighting Cancer</b><br/>Fighting Cancer: Targeting Cytotoxicity with Kinase Inhibitors<br/>Timothy D. Haffner - AstraZeneca</p> <p><b>6- Fighting Cancer</b><br/>Fighting Cancer: Targeting Cytotoxicity with Kinase Inhibitors<br/>Timothy D. Haffner - AstraZeneca</p> <p><b>7- Fighting Cancer</b><br/>Fighting Cancer: Targeting Cytotoxicity with Kinase Inhibitors<br/>Timothy D. Haffner - AstraZeneca</p> <p><b>8- Fighting Cancer</b><br/>Fighting Cancer: Targeting Cytotoxicity with Kinase Inhibitors<br/>Timothy D. 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| <p><b>Jan 31</b><br/><b>How to Succeed in Drug Discovery: Insight from Medicinal Chemists (1.5 hrs.)</b><br/>John Lowe III - JLL3 Pharm<br/>Mark Murcko - Relay Therapeutics<br/>Ann Weber - Kallyope<br/>William Greenlee - MedChem Discovery Consulting</p> <p><b>Feb 28</b><br/><b>Cosolvent Molecular Dynamics: Mapping Protein Surfaces to Discover Allosteric Sites</b><br/>Heather Carlson - University of Michigan<br/>Rommie Amaro - UC San Diego</p> <p><b>Mar 28</b><br/><b>Women at the Interface of Computational Chemistry and Drug Discovery (1.5 hrs)</b><br/>Zoe Cornia - Biomedical Research Foundation and JCM<br/>Kate Holloway - Gfree Bio<br/>Yvonne C. Martin - Previously of Abbott Laboratories<br/>Shana Posy - Bristol-Myers Squibb</p> <p><b>Apr 18</b><br/><b>Effective Exploration of Chemical Space in Hit-Finding</b><br/>Hanneke Jansen - Novartis Institutes for Biomedical Research<br/>Zoe Cornia - Biomedical Research Foundation and JCM</p> <p><b>May 30</b><br/><b>Widening the Therapeutic Window: Kinetic Selectivity and Target Vulnerability</b><br/>Peter Tonge - Stony Brook University and ACS Infectious Diseases<br/>Stewart Fisher - C4 Therapeutics</p> | <p><b>Jun 27</b><br/><b>Precision Control of CRISPR-Cas9</b><br/>Amit Choudhary - Broad Institute of Harvard and MIT<br/>Venkat Krishnamurthy - AstraZeneca</p> <p><b>Aug 8</b><br/><b>Transformation of Recombinant Cells to FDA Approved Products: Clinical Development to Marketplace (New Date)</b><br/>Rodney Ho - University of Washington<br/>Venkat Krishnamurthy - AstraZeneca</p> <p><b>Aug 22</b><br/><b>The Evolving Outsourcing Landscape in Pharma R&amp;D: Pros and Cons of Different Models</b><br/>Bart DeCorte - MercachemSyncom<br/>Allen Reitz - Fox Chase Chemical Diversity Center</p> <p><b>Sep 19</b><br/><b>Thinking Outside the Pillbox: Lead Generation and Optimization in Crop Protection Research</b><br/>Fides Benfatti - Syngenta</p> <p><b>Oct 24</b><br/><b>Treating Diabetes: Designing the Once-Weekly and Oral GLP-1</b><br/>Semaglutide<br/>Jesper Lau - Novo Nordisk A/S</p> <p><b>Nov 28</b><br/><b>Prodrugs</b><br/>Jarkko Rautio - University of Eastern Finland</p> |
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14



THIS ACS WEBINAR WILL BEGIN SHORTLY...

15



Treating Diabetes: Designing the Once-Weekly and Oral GLP-1 Semaglutide



**Puneet Tyagi**  
 Senior Scientist,  
 AstraZeneca



**Jesper Lau**  
 Vice President of Research Chemistry,  
 Novo Nordisk A/S

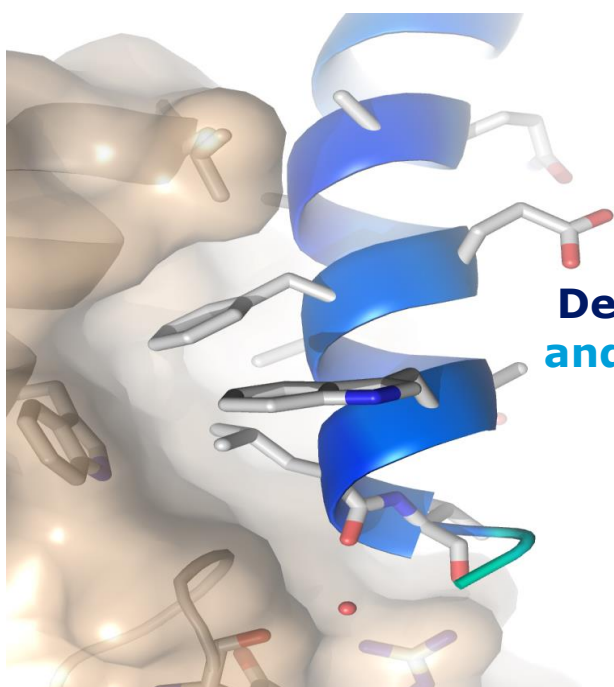
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17

## Designing the Once-Weekly and Oral GLP-1 Semaglutide

**Jesper Lau**  
Vice President  
Novo Nordisk



18

### Audience Survey Question

ANSWER THE QUESTION ON BLUE SCREEN IN ONE MOMENT



#### What is Glucagon-like-peptide-1?

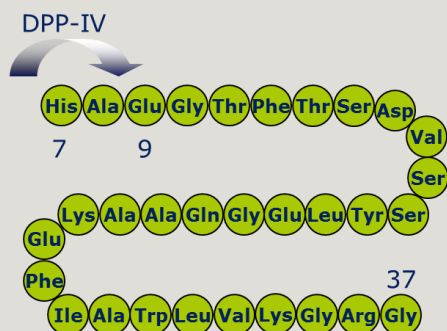
- A long acting artificial synthetic peptide
- A 32 amino acid natural peptide hormone
- A peptide released from the L-cells
- A peptide that increases appetite

*\* If your answer differs greatly from the choices above tell us in the chat!*

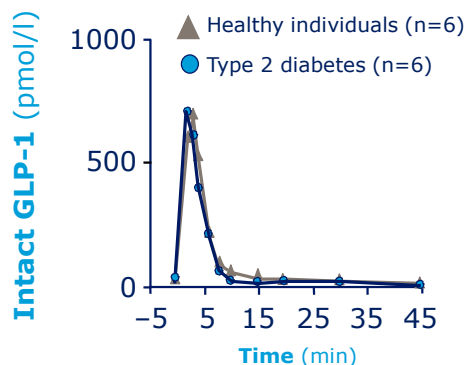


## Native GLP-1 has limited clinical value because of its short half-life

19



### i.v. bolus GLP-1 (15 nmol/l)



life-changing  
careers

Enzymatic cleavage  
High clearance (4–9 l/min)

$t_{1/2} = 1.5\text{--}2.1$  minutes  
(i.v. bolus 2.5–25.0 nmol/l)

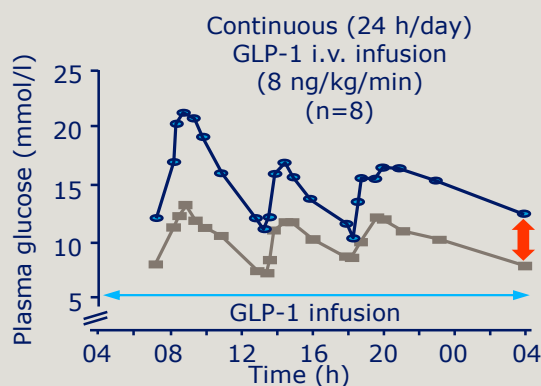
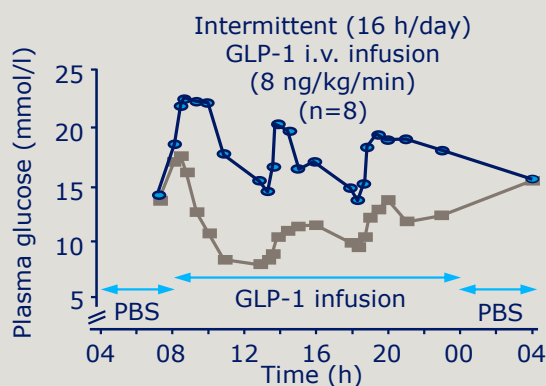


PK data adapted from Vilsbøll et al. J Clin Endocrinol Metab 2003;88:220–224



## Native GLP-1 must be administered continuously to realise full therapeutic potential

20



Blood glucose profiles: Day 0 Day 7

life-changing  
careers

Adapted from Larsen et al, Diabetes Care 2001;24:1416–1421.

PBS, phosphate-buffered saline.





## Discovery of the Insulinotropic Effect of GLP-1

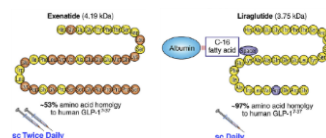
Bayliss and Starling proposed that intestinal mucosa contained a hormone which stimulated the exocrine secretion of the pancreas



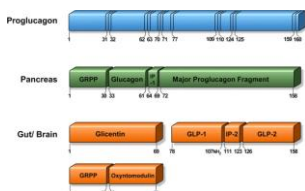
### Early clinical potential

Kreymann, Williams, Gbatei and Bloom, Lancet 1987;1300-1303  
Nathan, Schreiber, Fogel, Mojsov and Habener, Diabetes Care 1992;15(2):270-276  
Nauck, Klein, Ørskov, Holst, Willms and Creutzfeldt, Diabetologia 1993;36:741-744

### First two GLP-1 RA approvals 2005 and 2009

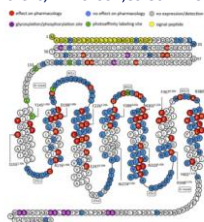


**Human proglucagon gene was cloned**  
Bell, Nature 1983;302:716-718

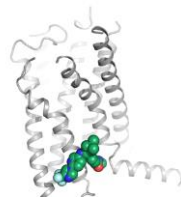


### GLP-1 receptor cloned

Thorens, PNAS 1992;89:8641-45



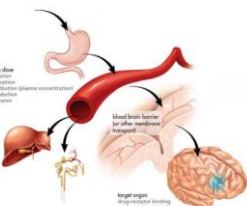
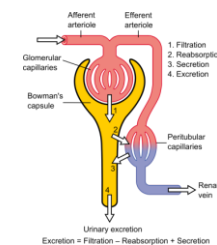
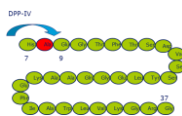
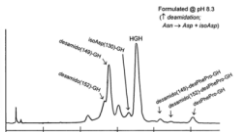
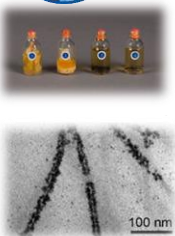
### GPCR class B structures



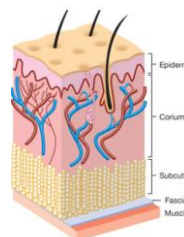
life-changing careers



## Key puzzle for successful GLP-1 engineering



life-changing careers

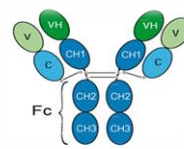
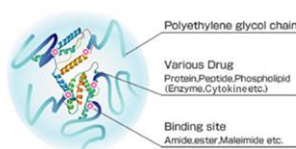
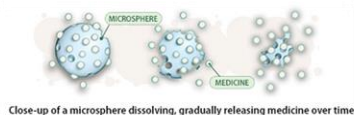




## Once weekly GLP-1: Parallel explorations of protraction enablers

### Several strategies have been explored by industry:

- **Sustained release:**
  - Bydureon (BMS/AstraZeneca), Taspoglutide (Roche/Ipsen)
- **Fusion proteins:**
  - Albiglutide (GSK)
  - Dulaglutide (GLP-1 Fc, LY2189265, Lilly)
  - GLP-1 transferrin (PF-4856883, Pfizer)
- **Pegylation:**
  - GLP-1 PEG (Lilly)
- **Reversible albumin binding**
  - **Semaglutide** (Novo Nordisk)



## Human serum albumin

- Is a large (>60kDa) natural human protein
- Circulates in the blood in high concentrations (~40mg/ml)
- Has a long plasma  $T_{1/2}$  (3 weeks)
- Binds fatty acids reversibly (transport and solubility)

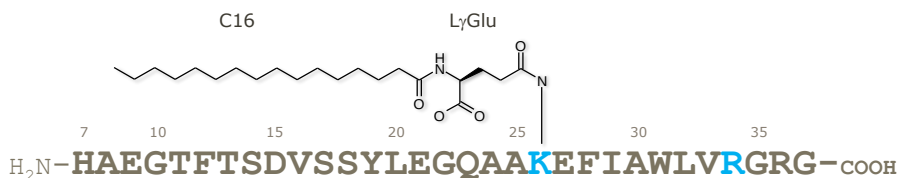






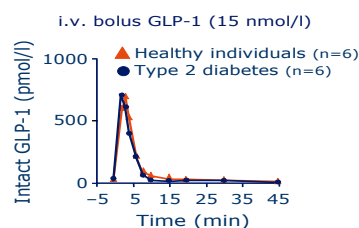
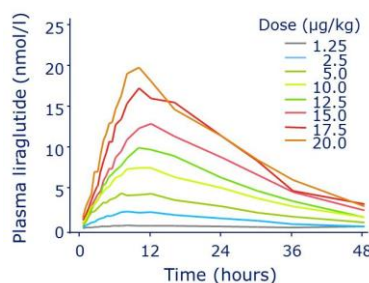
## Liraglutide obtains a once-daily profile by reversible binding to albumin

25



### PK parameters

- T<sub>max</sub>: 9–12 h
- T<sub>1/2</sub>: 11–15 h
- Bioavailability: 55%



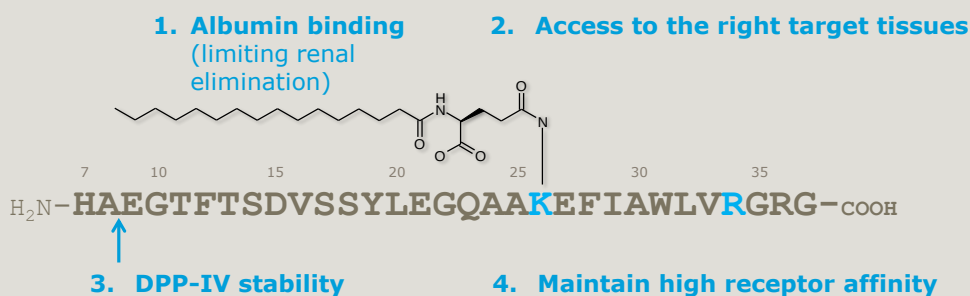
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Adapted from Elbrønd et al. Diabetes Care 2002;25:1398–1404. n=72 (n=8 for each dose)



## Four key hurdles to engineering a superior once - weekly GLP-1

26



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Lau, J. et al J. Med. Chem; 2015, 58, 7370–7380



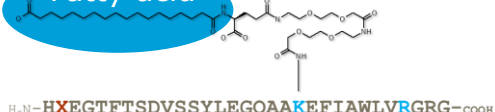


29



## Prolonging the half-life from once-daily to once-weekly by fatty acid exploration

Fatty acid



C16 acid

C12 diacid

C14 diacid

C16 diacid

C18 diacid

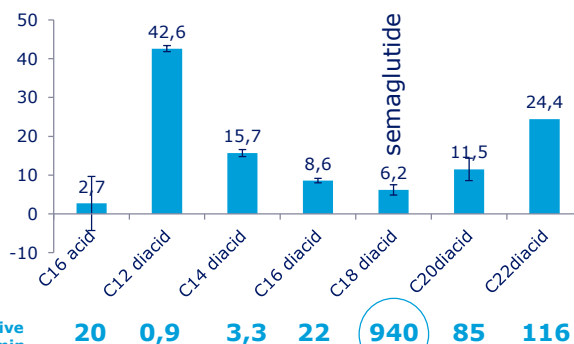
C20 diacid

C22 diacid

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Relative Albumin binding

GLP-1R potency (EC50 pM)



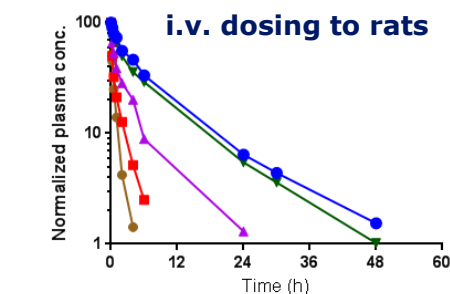
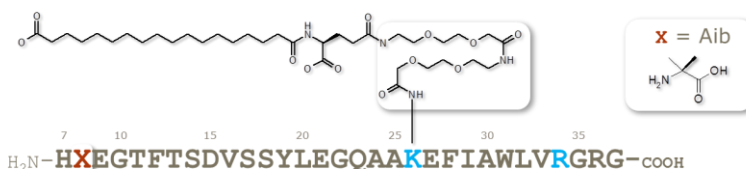
Lau, J. et al J. Med. Chem; 2015, 58, 7370-7380

30



## Systemic half-life increases

- with increasing length of di-acid



Semaglutide

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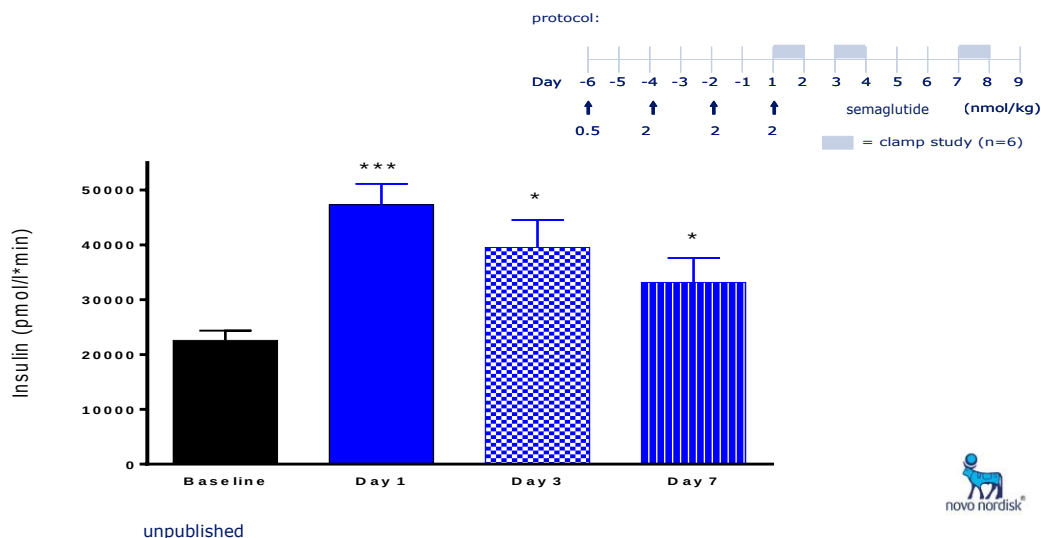
Lau, J. et al J. Med. Chem; 2015, 58, 7370-7380



## 7 Days duration of action of semaglutide

- in mini pigs, hyperglycaemic clamp

31

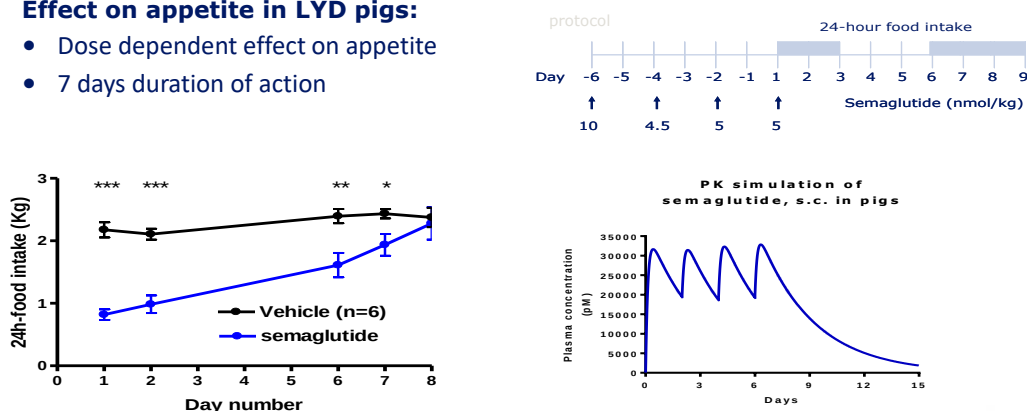


## Efficacy and duration of action of semaglutide

- in LYD pigs

32

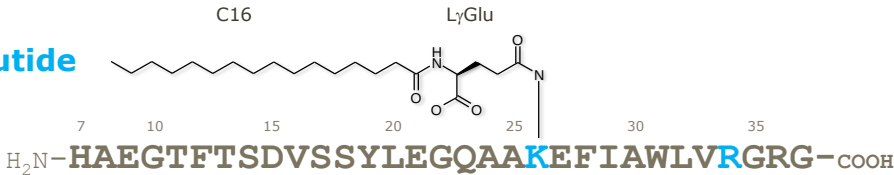
- Effect on appetite in LYD pigs:
  - Dose dependent effect on appetite
  - 7 days duration of action



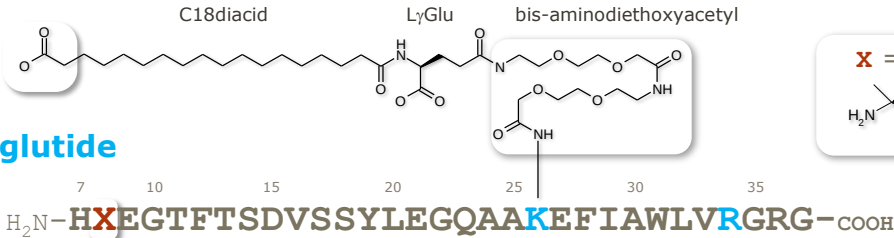


# GLP-1 Once-daily vs Once-Weekly - Minor Structural differences

## Liraglutide



## Semaglutide



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# Semaglutide was selected as once weekly lead - based on animal data

|                                       | Liraglutide | Semaglutide |
|---------------------------------------|-------------|-------------|
| Mini pig s.c. availability            | 66%         | 94%         |
| MRT minipig (s.c. dosing)             | 23hrs       | 64hrs       |
| In vivo potency (db/db mice)          | 6.9 nmol/kg | 0.3 nmol/kg |
| T <sub>1/2</sub> humans (s.c. dosing) | 13hrs       | ?           |
| Expected Human dose                   | <2mg/day    | <2mg/week   |

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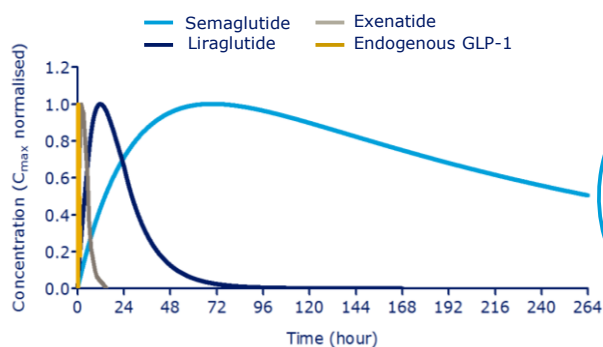




35



## Semaglutide has an optimal pharmacokinetic profile for once weekly dosing...



Simulation of pharmacokinetic profile

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**GLP-1 peptide with 2 substituted amino acids**

- protect against enzymatic degradation by DPP-4

**C-18 fatty di-acid**

- Strong albumin binding creates a circulating depot of active compound

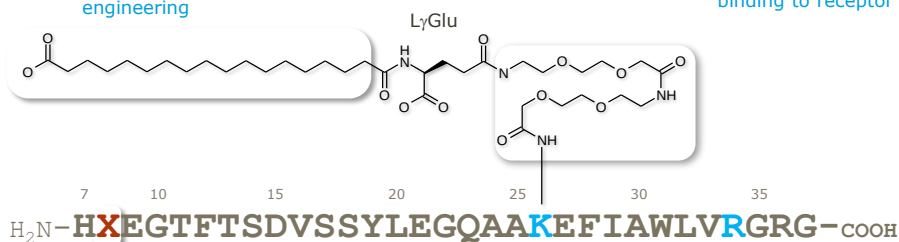
36



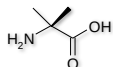
## Semaglutide is the result of a few smart modifications to the human GLP-1 molecule

Fatty acid optimisation for strong albumin binding.  
NN protein chemical engineering

OEG linker for peptide flexibility and optimised binding to receptor



**x = Aib**



Aib is an unnatural amino acid for preventing peptidase degradation

Peptide chain based on liraglutide discovery (human GLP-1):  
NN protein chemical engineering and alanine scan

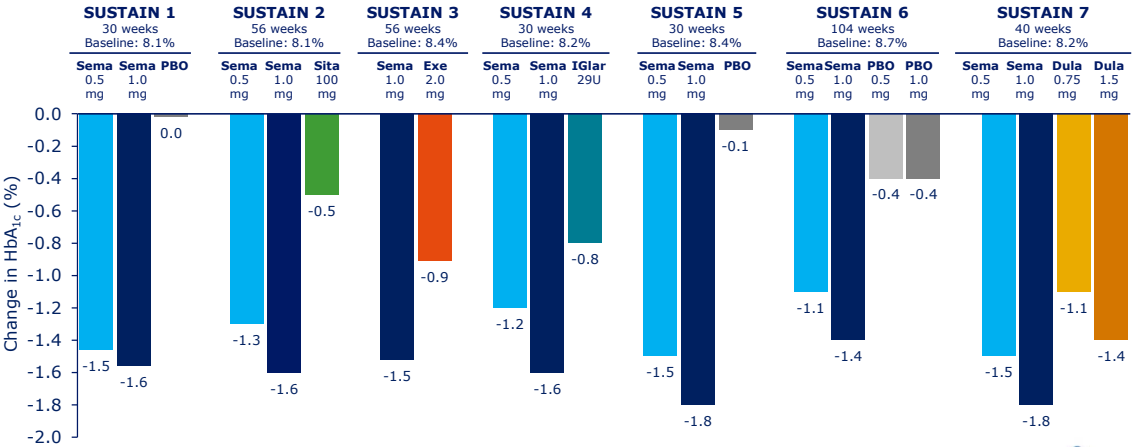
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37



# Once-weekly semaglutide provides unprecedented glucose regulation...



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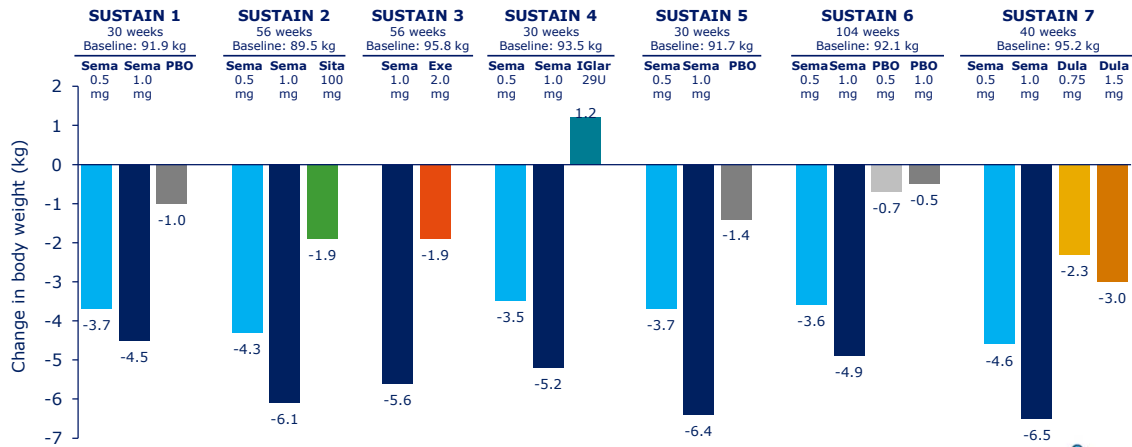
Dula: Dulaglutide (Trulicity®); Exe: exenatide (Bydureon®); IGlar: insulin glargine (Lantus®); PBO: placebo; Sita: sitagliptin



38



# ... and unprecedented weight loss



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Dula: Dulaglutide (Trulicity®); Exe: exenatide (Bydureon®); IGlar: insulin glargine (Lantus®); PBO: placebo; Sita: sitagliptin

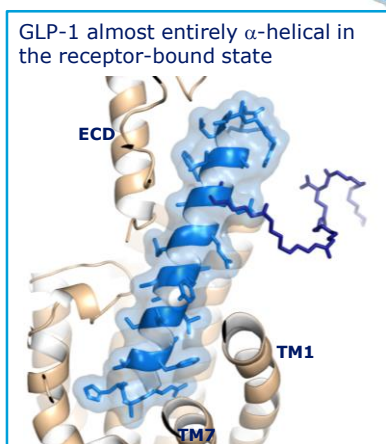




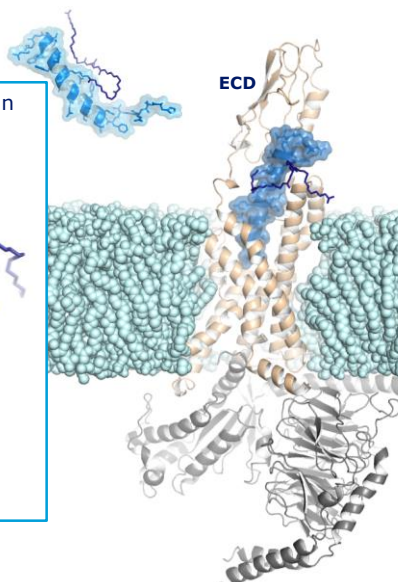
## ...and a highly selective binding to the human GLP-1 receptor

39

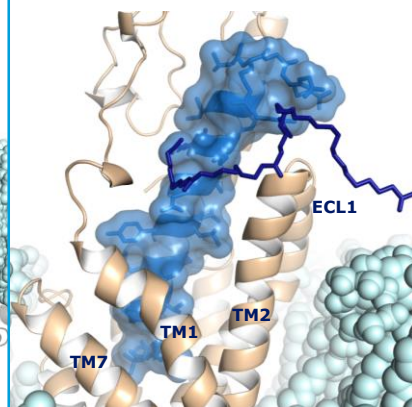
GLP-1 almost entirely  $\alpha$ -helical in the receptor-bound state



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Binding site defined primarily by ECD, ECL1, TM1, TM2 and TM7



novo nordisk

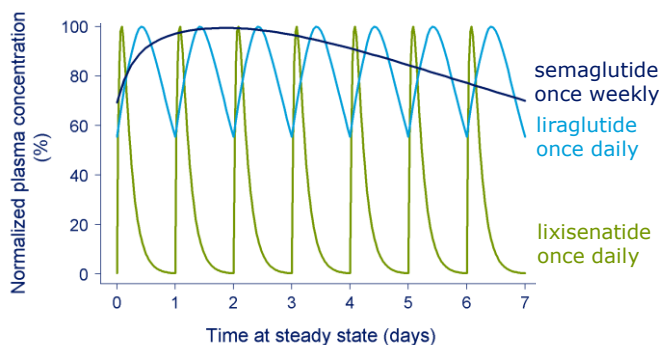


## Why is semaglutide different?

40

Continuous plasma exposure with little fluctuation and higher concentration in specific area of the appetite centre

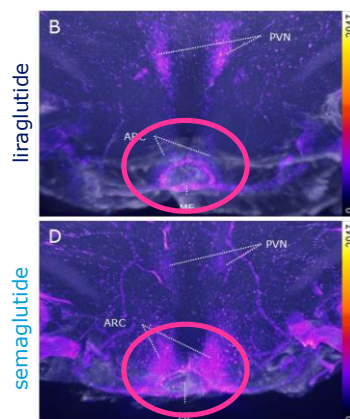
### Simulated pharmacokinetic profiles



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PK modelling  
Sources: Watson E, et al., *J. Clin. Pharm* 2010; 50: 886-894 (liraglutide), meta-analysis ClinPharm trials (semaglutide - data on file) and Frank T (2013) *J Pharm Drug Deliv Res.* 2013; 2:1 (lixisenatide)

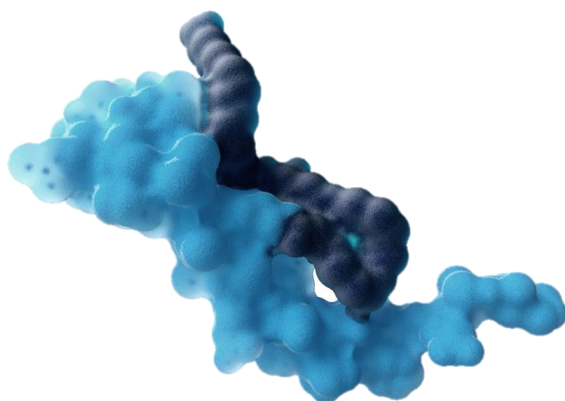
### Chronic administration





## Semaglutide - a convenient once-weekly GLP-1 with superior blood glucose regulation

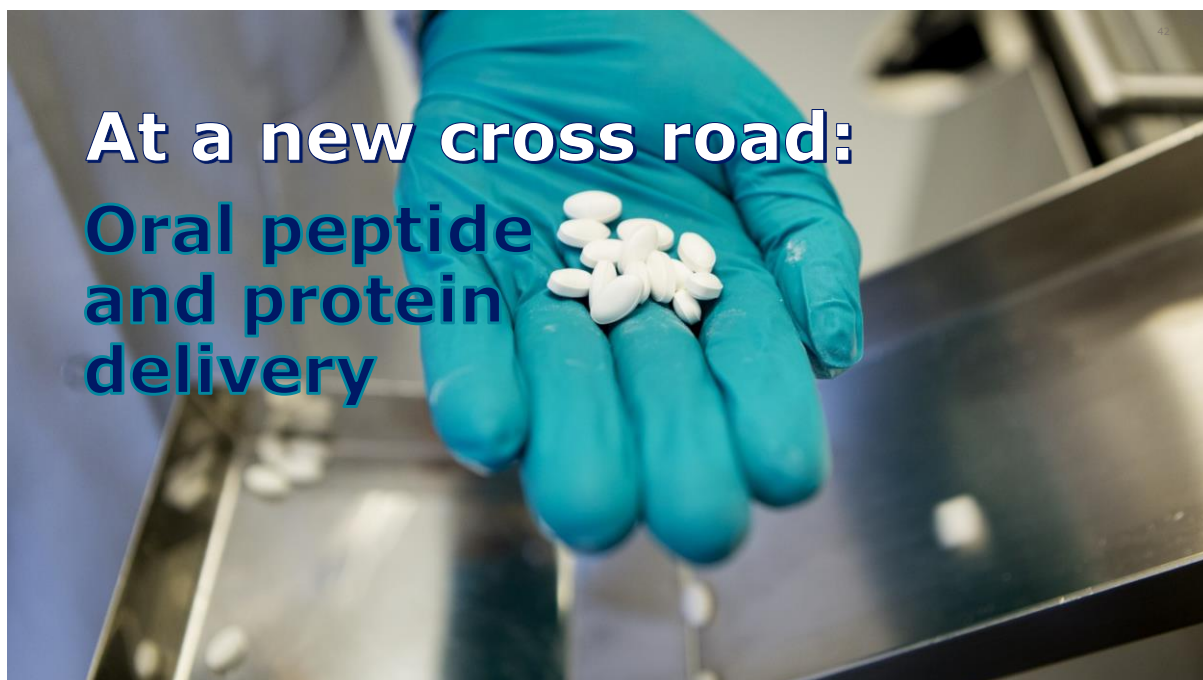
41



### Semaglutide

- is an analogue of human GLP-1
- has a once weekly profile through binding to albumin
- has a high potency and long duration of action in animals which translate to an excellent profile in humans
- holds great opportunity for oral administration

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42

## Audience Survey Question

ANSWER THE QUESTION ON BLUE SCREEN IN ONE MOMENT



**Which statement is wrong? Oral GLP-1 peptide delivery is a challenge due to:**

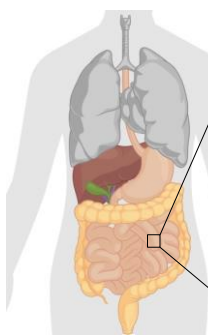
- Enzymatic degradation in the intestinal tract
- The intestinal uptake due to the size of the peptide
- The clinical trials are very difficult
- An absorption enhancer may be required

*\* If your answer differs greatly from the choices above tell us in the chat!*



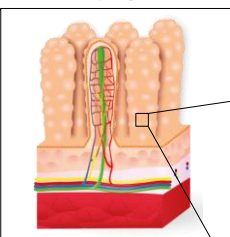
## There are many barriers to oral protein delivery

### Avoiding degradation



The gastro-intestinal tract is designed to degrade proteins by enzymes and low pH

### Reaching epithelial cells



### Absorption to blood



Proteins are lipophobic: no passive transport through the intestinal wall



## Oral delivery platforms

### Eligen®

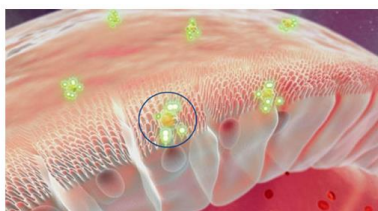
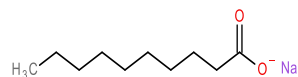


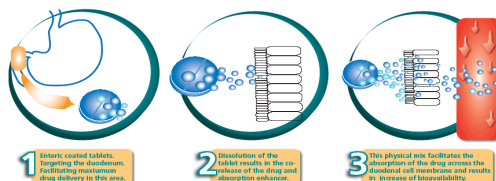
Fig. 1: Eligen Technology in action. As depicted inside the blue circle, delivery agents (small white dots) chaperone a therapeutic molecule (the green entity) entering into the outer membrane of an epithelial gastrointestinal cell. The gastrointestinal tract is on the top and the blood stream is on the bottom right

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### GIPET®



#### HOW DOES GIPET® WORK?

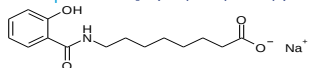


- Up to 46 Times more Drug Absorbed in Clinical Trials
- 26 Clinical Studies - Broad range drug types
- GMAA status simplifies development



## Understanding the absorption of oral semaglutide/SNAC tablets

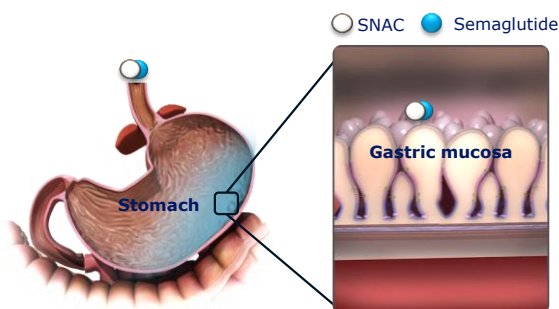
**SNAC** | Sodium N-[8-(2-hydroxybenzoyl)amino]caprylate



SNAC is an enhancer that facilitates absorption

The available data for semaglutide co-formulated with SNAC support that absorption takes place in the stomach in a localised buffered environment

The effect is strictly time- and size-dependent and occurs primarily via trans-cellular route



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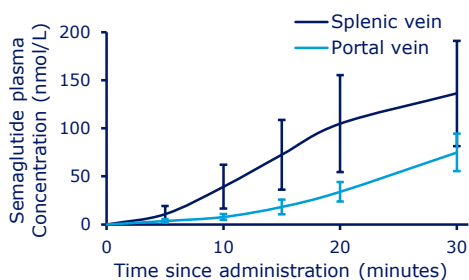




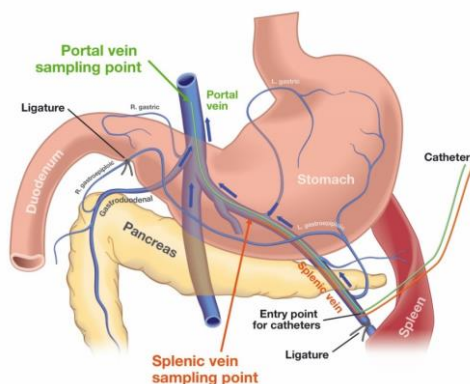
## Stomach is the predominant site of absorption

Highest concentration of semaglutide observed in vena linealis in dogs

### Plasma concentration of semaglutide after 10 mg oral dose in dogs



Semaglutide levels were higher in the splenic vein over the first 30 min after dosing ( $AUC_{0-30min}$  splenic/portal: 1.9)

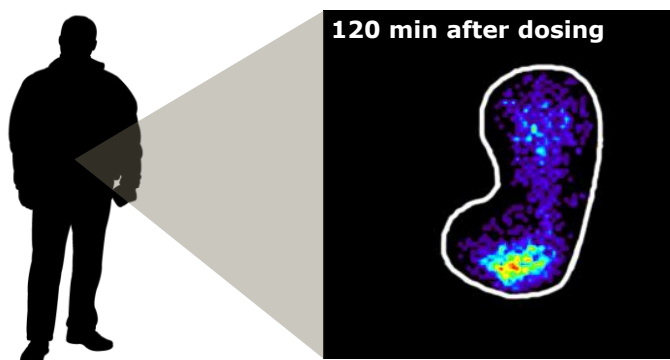


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## Complete tablet erosion of oral semaglutide occurs in the stomach

Scintigraphic imaging of an indium-111 labelled tablet



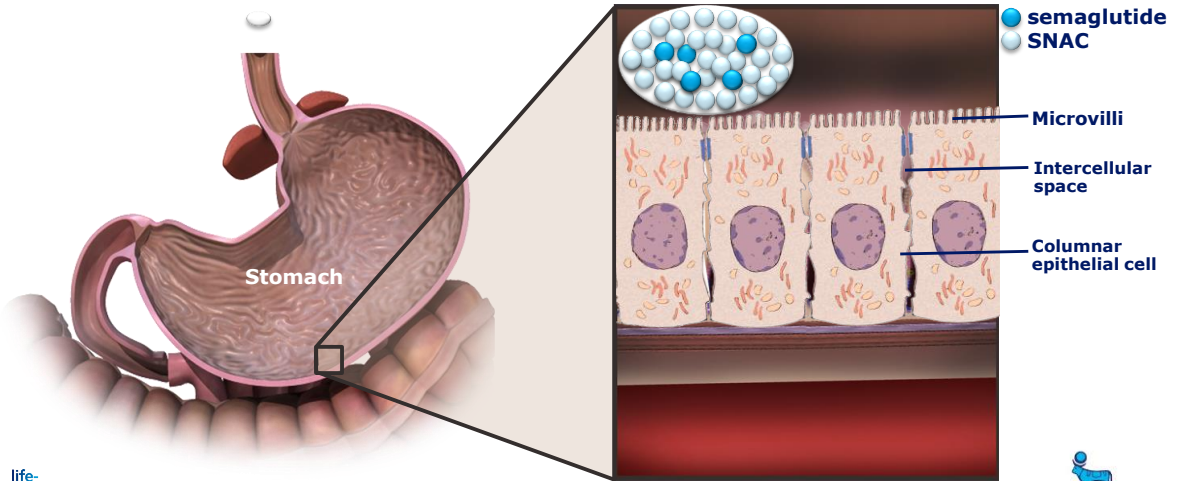
- Mean time to complete tablet erosion was 85 minutes (95% CI: [62;118])

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## SNAC carrier facilitates semaglutide absorption



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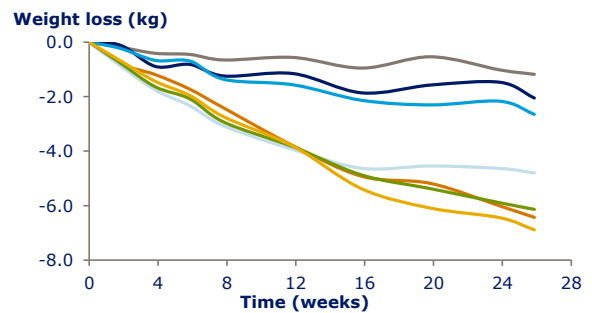
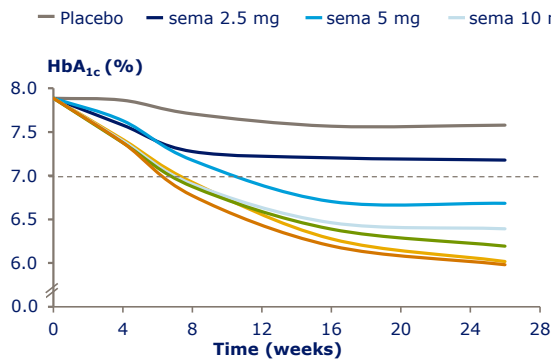
SNAC: Sodium N-[8-(2-hydroxybenzoyl) Amino] Caprylate



## Oral semaglutide dose dependently reduced HbA<sub>1c</sub> and body weight in phase 2 trial

HbA<sub>1c</sub> reduction from a mean baseline of 7.9%

Weight loss from a mean base line of 92 kg



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Data on graph are estimated mean  $\pm$  standard error of the mean  
SC: subcutaneous; Sema: semaglutide  
Main inclusion criteria: Type 2 diabetes;  $7.0\% \leq \text{HbA}_{1c} \leq 9.5\%$ ; Treatment with diet and exercise  
 $\pm$  metformin  
Source: Trial NN924-3790





## Conclusion

### Semaglutide:

- Is a once weekly GLP-1 analog that binds to albumin
- Is an analog of human GLP-1
- Was selected as once weekly candidate based on long duration of action in pigs
- Once weekly profile was confirmed in humans
- Has now shown great opportunity for both once weekly dosing and oral treatment



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Thanks to the Semaglutide Team



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**Puneet Tyagi**  
Senior Scientist,  
AstraZeneca



**Jesper Lau**  
Vice President of Research Chemistry,  
Novo Nordisk A/S

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53

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| 2014                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   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| <p><b>Drug Discovery Series #1: Current Drug Discovery and Development Process</b><br/>QD1 #1: Overview of the drug discovery and development process to learn the stages and challenges in every step.</p> <p><b>Primer to Drug Target Classes</b><br/>QD1 #2: Listen in on a discussion on the big four drug target families and the difference between small molecule and biopharmaceutical targets.</p> <p><b>Key Concepts in Identifying Drug Leads</b><br/>QD1 #3: Discover how drug classes in a desecrating context explore the flag of flag, and those that slipped from the past may guide the present.</p> <p><b>Lead Optimization - Building Efficacy &amp; Safety</b><br/>QD1 #4: Learn strategies to how to effectively optimize your molecule and rapidly assess your findings.</p> <p><b>Time for Filing IND and Starting your Clinical Trials</b><br/>QD1 #5: What do you need to know when filing for investigational New Drug submissions to the United States Food and Drug Administration?</p> <p><b>The Role of Chemistry in Clinical Trials: The Big Expense &amp; Lessons Learned</b><br/>QD1 #6: Learn how the properties of the candidate impact decisions in the discovery process.</p> <p><b>Pharmacokinetics and IP Strategies in Drug Development</b><br/>QD1 #7: Review the basic principles of pharmacokinetics in drug development strategies as well as to risk in determining health insurance coverage of drug products.</p> <p><b>Future of Drug Discovery - Challenges, Risks and Rewards</b><br/>QD1 #8: Explore how new risks and challenges will be met with in the future and the key role required of future medicinal chemists.</p> | <p><b>Designing Better Drug Candidates</b><br/>QD1 #9: Learn how medicinal chemists can be used to improve candidate quality from the start.</p> <p><b>Strategies to Improve Solubility of Drug Candidates</b><br/>QD1 #10: Learn a number of different strategies for improving drug solubility through structural modification.</p> <p><b>Program-Based Drug Design Strategies</b><br/>QD1 #11: Discover the right drug design strategy for your target. Learn how to focus on the major problem and working results.</p> <p><b>Screening Strategies</b><br/>QD1 #12: Learn the pros and cons of different screening strategies.</p> <p><b>Avoiding PKCδ (protein kinase C) inhibition</b><br/>QD1 #13: Learn how to avoid some PKCδ inhibition to avoid the loss of drug discovery.</p> <p><b>Advancing CMC: From Process Development to Production</b><br/>QD1 #14: Learn how to avoid some PKCδ inhibition to avoid the loss of drug discovery.</p> <p><b>From Concept to Drug Development</b><br/>QD1 #15: Learn how to avoid some PKCδ inhibition to avoid the loss of drug discovery.</p> <p><b>Chemical Space in Drug Design: From Selection to Optimization</b><br/>QD1 #16: Learn how to avoid some PKCδ inhibition to avoid the loss of drug discovery.</p> <p><b>Delivery Systems to Support Drug Development in Preclinical and Clinical Studies</b><br/>QD1 #17: Learn how to avoid some PKCδ inhibition to avoid the loss of drug discovery.</p> <p><b>Pharmacokinetics Considerations in Drug Design and Development</b><br/>QD1 #18: Learn how to avoid some PKCδ inhibition to avoid the loss of drug discovery.</p> <p><b>Primer to Drug Target Classes</b><br/>QD1 #19: Learn how to avoid some PKCδ inhibition to avoid the loss of drug discovery.</p> | <p><b>1 - Time: The Fourth Dimension in Drug Discovery</b><br/>QD1 #20: Learn how to avoid some PKCδ inhibition to avoid the loss of drug discovery.</p> <p><b>The Importance of Drug Target Kinetics in Drug Design</b><br/>QD1 #21: Learn how to avoid some PKCδ inhibition to avoid the loss of drug discovery.</p> <p><b>Long Acting Injectable Medications: Strategies and Mechanisms</b><br/>QD1 #22: Learn how to avoid some PKCδ inhibition to avoid the loss of drug discovery.</p> <p><b>Modular Protein Formulations for Solubility Targeted Compounds</b><br/>QD1 #23: Learn how to avoid some PKCδ inhibition to avoid the loss of drug discovery.</p> <p><b>The Molecular Character of Tumor (Special Topic)</b><br/>QD1 #24: Learn how to avoid some PKCδ inhibition to avoid the loss of drug discovery.</p> <p><b>Design of Deliverable Monoclonal Antibodies</b><br/>QD1 #25: Learn how to avoid some PKCδ inhibition to avoid the loss of drug discovery.</p> <p><b>Designing and Testing Thinking Small: Applying Medicinal Chemistry Strategy to Antibody Drug Candidates</b><br/>QD1 #26: Learn how to avoid some PKCδ inhibition to avoid the loss of drug discovery.</p> <p><b>Biological Activity: Therapeutic Making Sense of Antibody</b><br/>QD1 #27: Learn how to avoid some PKCδ inhibition to avoid the loss of drug discovery.</p> <p><b>Cryopreservation in Drug Design and Development</b><br/>QD1 #28: Learn how to avoid some PKCδ inhibition to avoid the loss of drug discovery.</p> <p><b>Designing with Flexible Drug Candidates in Drug Development</b><br/>QD1 #29: Learn how to avoid some PKCδ inhibition to avoid the loss of drug discovery.</p> <p><b>Rational Design of Small Molecule Targeting RNA</b><br/>QD1 #30: Learn how to avoid some PKCδ inhibition to avoid the loss of drug discovery.</p> <p><b>Cell Penetrating Peptides to Improve Cellular Drug Uptake</b><br/>QD1 #31: Learn how to avoid some PKCδ inhibition to avoid the loss of drug discovery.</p> | <p><b>1 - 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54



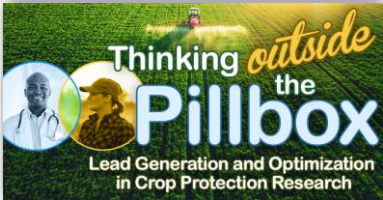
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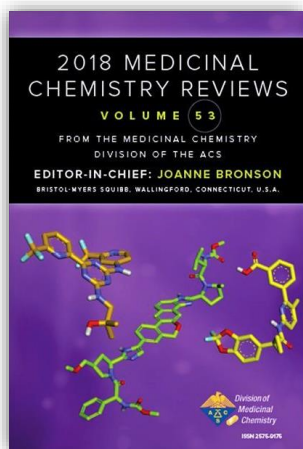
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